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EXAMINER	
REIDEL, JESSICA L	
ART UNIT	**PAPER NUMBER**
3766	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,937	SHAFER, LISA LYNN	
	Examiner	Art Unit	
	Jessica L. Reidel	3766	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,21-33,35,36,43,44,48-53,58-63 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,21-33,35,36,43,44,48-53,58-63 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of Applicant's Amendment, which was received by the Office on November 17, 2006. Claims 19-20, 34, 37-42, 45-47, 54-57, 60, 64-67 and 69 have been cancelled. Claims 1-18, 21-33, 35-36, 43-44, 48-53, 58-63 and 68 are pending.

Response to Amendment

2. The declaration filed on November 17, 2006 under 37 CFR 1.131 is sufficient to overcome the Yun et al. (U.S. 2004/0249416) reference.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. ***Claims 1-13, 21, 23-24, 27-31, 35 and 59 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rezai (U.S. 2002/0116030).*** As to Claims 1-2, 5 and 21, Rezai discloses a method comprising stimulating a sympathetic neuron of a mammalian subject in an amount effective to inhibit the release of a proinflammatory mediator (see Rezai Abstract, page 1, paragraphs 4-7 and page 2, paragraphs 14 and 19). The Examiner takes the position that the oscillating electrical signal comprising a plurality of electrical pulses of the Rezai method, operated at a frequency range between about 2

Hz and 2500 Hz, having a voltage between about 0.1 μV to about 20V and a pulse width between 10 microseconds to about 1,000 microseconds is synonymous with an "amount effective to inhibit the release of a proinflammatory mediator" due to Applicant's disclosure pages 17 and 26-28 (see Rezai page 2, paragraph 19 and page 5, paragraph 38). The Examiner also notes that although the method of Rezai is not explicitly disclosed "to inhibit the release of a proinflammatory mediator", the oscillating electrical signal comprising a plurality of electrical pulses of the Rezai method is capable of inhibiting the release of a proinflammatory mediator and "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of an unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ430, 433 (CCPA 1977) (MPEP § 2112).

Rezai discloses that the cell is a sympathetic neuron in a patient suffering from, or at risk for disease or disorder such as burns or spinal cord injury (see Rezai page 7, paragraphs 50-51). It is inherent that these diseases or disorders are mediated by an inflammatory cytokine cascade and the Examiner makes reference to Applicant's disclosure pages 8-12 (see Rezai page 1, paragraphs 9-10, page 2, paragraphs 10-11, page 3, paragraphs 26-30, page 5, paragraphs 44-45, page 6, paragrapsh 46-48 and 50, page 7, paragraphs 50-56 and page 8, paragraphs 59-69). It is also inherent, or at least obvious to one having ordinary skill in the art at the time the invention was made that a physician, nurse or equivalent would have "identified a mammalian subject suffering from, or at risk for, such diseases" before administering any stimulation of sympathetic

neurons otherwise the physician, nurse or equivalent would be treating patients who do not even need treatment.

5. As to Claims 3-4, Rezai discloses that the electrode 122, used to stimulate the sympathetic neuron of interest, is coupled to a pulse generator, which may be implanted on or adjacent to the electrode 122 (see Rezai page 4, paragraph 37).

6. As to Claims 6-8, Rezai discloses that the electrode 122 may be used to electrically stimulate any cervical ganglion or ganglia, thoracic ganglion or ganglia, lumbar ganglion or ganglia or sacral ganglia or any combination thereof associated with a particular physiological disorder to be affected, modulated, treated, alleviated or ameliorated (see Rezai page 1, paragraph 5). The Examiner takes the position that these "ganglion or ganglia" disclosed by Rezai comprise neurons of the splenic nerve and makes reference to Applicant's disclosure pages 17-18.

7. As to Claims 9-10, Rezai discloses that the stimulation comprises an oscillating electrical signal, comprising a plurality of electrical pulses, operated at a frequency range between about 2 Hz and 2500 Hz, having a voltage between about 0.1 μV to about 20V and a pulse width between 10 microseconds to about 1,000 microseconds (see Rezai page 2, paragraph 19 and page 5, paragraph 38).

8. As to Claims 11-12, Rezai discloses that the electrode 122, used to stimulate the sympathetic neuron of interest, is coupled to a pulse generator, which may be implanted on or adjacent to the electrode 122 (see Rezai page 4, paragraph 37).

9. As to Claim 13, Rezai discloses that the plurality of electrical pulses are applied to the neuron (see Rezai page 1, paragraphs 2, 4-5 and 9).

10. As to Claim 23, Rezai discloses that the method is capable of effecting a variety of physiological disorders or pathological conditions by placing an electrode 122 adjacent to or in communication with at least one ganglion along the sympathetic nerve chain and stimulating the at least one ganglion until the physiological disorder or pathological condition has been effected (see Rezai Abstract, page 1, paragraphs 4-5 and page 4, paragraph 36).

11. As to Claim 24, Rezai discloses that postganglionic sympathetic nerve fibers converge, in small nodes of nerve cells, called ganglia (see Rezai page 3, paragraph 28) and further discloses that the method may comprise stimulation any cervical ganglia, thoracic ganglia, lumbar ganglia or sacral ganglia or combination thereof (see Rezai page 1, paragraph 5).

12. As to Claims 27, 35 and 59, Rezai discloses a method comprising stimulating a sympathetic neuron in a patient in an amount sufficient to inhibit the inflammatory cytokine cascade (see Rezai Abstract, page 1, paragraphs 4-7 and page 2, paragraphs 14 and 19). The Examiner takes the position that the oscillating electrical signal, comprising a plurality of electrical pulses of the Rezai method operated at a frequency range between about 2 Hz and 2500 Hz, having a voltage between about 0.1 μV to about 20V and a pulse width between 10 microseconds to about 1,000 microseconds is synonymous with an "amount sufficient to inhibit the inflammatory cytokine cascade" due to Applicant's disclosure pages 17 and 26-28 (see Rezai page 2, paragraph 19 and page 5, paragraph 38). The Examiner also notes that although the method of Rezai is not explicitly disclosed "to inhibit the inflammatory cytokine cascade", the oscillating electrical signal comprising a plurality of electrical pulses of the Rezai method is capable of inhibiting the inflammatory cytokine cascade and "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's

functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of an unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ430, 433 (CCPA 1977) (MPEP § 2112).

Rezai discloses that the cell is a sympathetic neuron in a patient suffering from, or at risk for disease or disorder such as burns or spinal cord injury (see Rezai page 7, paragraphs 50-51). It is inherent that these diseases or disorders are mediated by an inflammatory cytokine cascade and the Examiner makes reference to Applicant's disclosure pages 8-12 (see Rezai page 1, paragraphs 9-10, page 2, paragraphs 10-11, page 3, paragraphs 26-30, page 5, paragraphs 44-45, page 6, paragrapsh 46-48 and 50, page 7, paragraphs 50-56 and page 8, paragraphs 59-69). It is also inherent, or at least obvious to one having ordinary skill in the art at the time the invention was made that a physician, nurse or equivalent would have "identified and/or diagnosed a mammalian subject suffering from, or at risk for, such diseases" before administering any stimulation of sympathetic neurons otherwise the physician, nurse or equivalent would be treating patients who do not even need treatment.

13. As to Claim 28, Rezai discloses that an electrode 122, coupled to a pulse generator is used to stimulate the sympathetic neuron of interest (see Rezai page 4, paragraph 37).

14. As to Claim 29, Rezai discloses that the method is capable of effecting a variety of physiological disorders or pathological conditions by placing an electrode 122 adjacent to or in communication with at least one ganglion along the sympathetic nerve chain and stimulating the

at least one ganglion until the physiological disorder or pathological condition has been effected (see Rezai Abstract, page 1, paragraphs 4-5 and page 4, paragraph 36).

15. As to Claim 30, Rezai discloses that postganglionic sympathetic nerve fibers converge, in small nodes of nerve cells, called ganglia (see Rezai page 3, paragraph 28) and further discloses that the method may comprise stimulation any cervical ganglia, thoracic ganglia, lumbar ganglia or sacral ganglia or combination thereof (see Rezai page 1, paragraph 5).

16. As to Claim 31, Rezai discloses that the electrode 122 may be used to electrically stimulate any cervical ganglion or ganglia, thoracic ganglion or ganglia, lumbar ganglion or ganglia or sacral ganglia or any combination thereof associated with a particular physiological disorder to be affected, modulated, treated, alleviated or ameliorated (see Rezai page 1, paragraph 5). The Examiner takes the position that these "ganglion or ganglia" disclosed by Rezai comprise neurons of the splenic nerve and makes reference to Applicant's disclosure pages 17-18.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. ***Claims 25 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rezai.*** Rezai discloses the claimed invention as discussed above except that the method does not further comprise direct stimulation of a peripheral tissue or organ served by the splenic nerve. It

would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method as taught by Rezai with direct stimulation of a peripheral tissue or organ served by the splenic nerve, because Applicant has not disclosed that such stimulation provides an advantage, is used for a particular purpose, or solves a stated problem. One of ordinary skill in the art, furthermore, would have expected applicant's invention to perform equally well with the sympathetic nerve stimulation as taught by Rezai, because it stimulation in an amount effective to inhibit the release of a proinflammatory mediator and since it appears to be an arbitrary design consideration which fails to patentably distinguish over Rezai.

Therefore, it would have been an obvious matter of design choice to modify Rezai to obtain the invention as specified in the claim(s).

19. ***Claims 14-18, 26 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rezai in view of Tracey (U.S. 6,610,713).*** As to Claims 14-17, Rezai discloses the claimed invention as discussed above except that the inhibition of a profinflammatory mediator is not specified to be inhibition of an inflammatory cytokine called TNF-α. Tracey, however, teaches that inflammation and other deleterious conditions (such as ischemia) are often induced by proinflammatory cytokines such as tumer necrosis factor (TNF-α) (see Tracey columns 1-2). Since the method of Rezai is specified for use in treating ischemia in addition to burns and spinal cord injury (see Rezai pages 5-7), it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of King in view of Tracey to comprise inhibition of the inflammatory cytokine TNF-α in order to treat ischemia.

20. As to Claim 18, Rezai discloses the claimed invention as discussed above except that the proinflammatory mediator is not specified to be a chemokine. Tracey, however, teaches a

method of stimulating a nerve to inhibit the release of a pro-inflammatory cytokine such as IL-8. IL-8 is produced in acute and chronic inflammation to mobilize and activate white blood cells so it is inherent that inhibition of IL-8 inhibits the mobilization and activation of white blood cells during acute and chronic inflammation. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Rezai in view of Tracey to comprise inhibition of the inflammatory chemokine such as IL-8 in order to stop the mobilization and/or activation of white blood cells during acute and chronic inflammatory responses (such as ischemia) in a patient.

21. As to Claims 26 and 33, Rezai discloses the claimed invention as discussed above except that the method does not further comprise stimulating a vagus nerve. Tracey, however, discloses a method for inhibiting the release of a pro-inflammatory cytokine from a mammalian cell comprising stimulating a neuron (i.e. the vagus nerve) of a mammalian subject in an amount effective to inhibit the release of the pro-inflammatory cytokine (see Tracey column 10, lines 17-56) to treat a wide variety of diseases or disorders that are mediated by an inflammatory cytokine cascade such as organ ischemia. Tracey teaches that stimulation of the parasympathetic nervous system promotes release of acetylcholine, which inhibits release of a proinflammatory mediaor (see Tracey columns 1-2, column 3, lines 7-67, column 4, lines 1-67, column 5, lines 1-16, column 10, lines 17-67 and column 11, lines 1-30). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Rezai in view of Tracey to not only use electrical stimulation to inhibit sympathetic activity/outflow but to also include stimulating the vagus nerve inhibit an inflammatory cytokine cascade to better the invention.

22. ***Claims 1-13, 23-25 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over King (U.S. 6,058,331).*** As to Claims 1 and 27, King discloses a method comprising stimulating a sympathetic neuron of a mammalian subject in an amount effective to inhibit the release of a proinflammatory mediator/inhibit the inflammatory cytokine cascade. King specifies that the method is used for improving blood flow, for helping to restore tissue health and for treating organ ischemia using spinal cord or peripheral nerve electrical stimulation with closed loop feedback control (see King Title and Abstract) comprising the steps of identifying a mammalian subject suffering from organ ischemia using external sensor 30 or internal sensor 40 (see King column 5, lines 31-67 and column 6, lines 1-54) and stimulating a sympathetic neuron (either in the spinal cord or the peripheral nervous system) of the subject (see King Title, Abstract, Figs. 1-3, columns 1-2, column 3, lines 28-60, column 4, lines 29-67, column 5, lines 1-67, column 7, lines 41-56 and column 10, lines 8-59). It is inherent that organ ischemia is a disease or disorder that is mediated by an inflammatory cytokine cascade and the Examiner makes reference to Applicant's disclosure pages 8-12.

The Examiner takes position that the plurality of electrical pulses delivered by lead 16 of King -- having amplitudes of 0.1 to 20 volts, pulse widths varying from 60 to 1000 microseconds and repetition rates varying from 5 to 185 Hz or more -- is synonymous with an "amount effective to inhibit the release of a proinflammatory mediator" due to Applicant's disclosure pages 17 and 26-28 (see King column 10, lines 8-24). King specifies that the method may be used to inhibit sympathetic activity/outflow (see King column 5, lines 28-31, column 7, lines 42-56 and column 10, lines 8-24). Since sympathetic nervous activity inherently is a major controller/contributor to the neurogenic contribution to inflammation in the body, a method that

inhibits such sympathetic nervous activity (such as the method of King) inherently inhibits release of a proinflammatory cytokine cascade.

The Examiner also notes that although the method of King is not explicitly disclosed "to inhibit the release of a proinflammatory mediator" or to "inhibit the inflammatory cytokine cascade", the electrical pulses delivered by lead 16 of the King method are capable of inhibiting the release of a proinflammatory mediator /the inflammatory cytokine cascade for the reasons discussed above and "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of an unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ430, 433 (CCPA 1977) (MPEP § 2112).

King discloses the claimed invention as discussed above except that it is not specified that the method be used to treat cerebral infarction. Since King does disclose at column 7, lines 42-56 that the method "may be utilized to improve blood flow in other parts of the body in addition to the limbs including, for example, human organs" and further that the method may be used to "prevent tissue degeneration" and "maintain a constant tissue blood flow" it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the method of King to treat cerebral infarction. It is well known in the art that cerebral infarction is caused by ischemia (i.e. disturbed perfusion or lack of blood flow to the brain which causes cells to die or be seriously damaged).

23. As to Claims 2-5 and 28, King discloses that an implanted stimulation electrode delivers a plurality of electrical pulses to a sympathetic neuron via an implantable signal generator 14 (see King Figs. 1-3, column 3, lines 44-48, column 4, lines 29-67, column 5, lines 1-31 and column 10, lines 8-24).

24. As to Claims 6-13, 23-24 and 29-31, in addition to the arguments presented above, King discloses that lead 18 may have stimulation electrodes that may be positioned at spinal vertebral levels T8-L1. It is inherent that the splenic nerve is located at these vertebral levels. It is inherent that postganglionic sympathetic nerve fibers converge, in small nodes of nerve cells, called ganglia and King specifies that the stimulation lead 18 may also be position adjacent to the lumbar sympathetic ganglia (see King column 4, lines 66-67 and column 5, lines 1-31).

25. As to Claims 25 and 32, King discloses the claimed invention as discussed above except that the method does not further comprise direct stimulation of a peripheral tissue or organ served by the splenic nerve. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method as taught by King with direct stimulation of a peripheral tissue or organ served by the splenic nerve, because Applicant has not disclosed that such stimulation provides an advantage, is used for a particular purpose, or solves a stated problem. One of ordinary skill in the art, furthermore, would have expected applicant's invention to perform equally well with the sympathetic nerve stimulation as taught by King, because the stimulation is in an amount effective to inhibit the release of a proinflammatory mediator and since it appears to be an arbitrary design consideration which fails to patentably distinguish over King.

Therefore, it would have been an obvious matter of design choice to modify King to obtain the invention as specified in the claim(s).

26. ***Claims 14-18, 26 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over King in view of Tracey.*** As to Claims 14-17, King discloses the claimed invention as discussed above except that the inhibition of a proinflammatory mediator is not specified to be inhibition of an inflammatory cytokine called TNF-α. Tracey, however, teaches that inflammation and other deleterious conditions (such as ischemia) are often induced by proinflammatory cytokines such as tumer necrosis factor (TNF-α) (see Tracey columns 1-2). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of King in view of Tracey to comprise inhibition of the inflammatory cytokine TNF-α in order to treat ischemia.

27. As to Claim 18, King discloses the claimed invention as discussed above except that the proinflammatory mediator is not specified to be a chemokine. Tracey, however, teaches a method of stimulating a nerve to inhibit the release of a pro-inflammatory cytokine such as IL-8. IL-8 is produced in acute and chronic inflammation to mobilize and activate white blood cells so it is inherent that inhibition of IL-8 inhibits the mobilization and activation of white blood cells during acute and chronic inflammation. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of King in view of Tracey to comprise inhibition of the inflammatory chemokine such as IL-8 in order to stop the mobilization and/or activation of white blood cells during acute and chronic inflammatory responses (such as ischemia) in a patient.

28. As to Claims 26 and 33, King discloses the claimed invention as discussed above except that the method does not further comprise stimulating a vagus nerve. Tracey, however, discloses a method for inhibiting the release of a pro-inflammatory cytokine from a mammalian cell comprising stimulating a neuron (i.e. the vagus nerve) of a mammalian subject in an amount effective to inhibit the release of the pro-inflammatory cytokine (see Tracey column 10, lines 17-56) to treat a wide variety of diseases or disorders that are mediated by an inflammatory cytokine cascade such as organ ischemia. Tracey teaches that stimulation of the parasympathetic nervous system promotes release of acetylcholine, which inhibits release of a proinflammatory mediaor (see Tracey columns 1-2, column 3, lines 7-67, column 4, lines 1-67, column 5, lines 1-16, column 10, lines 17-67 and column 11, lines 1-30). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of King in view of Tracey to not only use electrical stimulation to inhibit sympathetic activity/outflow but to also include stimulating the vagus nerve inhibit an inflammatory cytokine cascade to better the invention.

29. ***Claims 1-2, 14-18, 21-22, 26-28, 33, 35-36, 43-44, 48-53, 58-59, 61-63 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tracey in view of Sherwood "Human Physiology: From Cells to Systems".*** As to Claims 1-2, 14, 21-22, 26-28, 33, 35-36, 43-44, 48-53, 58-59, 61-63 and 68, Tracey discloses a method for inhibiting the release of a pro-inflammatory cytokine from a mammalian cell/for inhibiting the inflammatory cytokine cascade comprising stimulating a neuron of a mammalian subject in an amount effective to inhibit the release of the pro-inflammatory cytokine (see Tracey column 10, lines 17-56). Tracy specifies that the cell is in a patient suffering from, or at risk for, a condition mediated by an inflammatory

cytokine cascade such as endotoxic shock, allergy, anaphylactic shock, sepsis, septicemia, cachexia, septic abortion, disseminated bacteremia, burns, Rheumatoid arthritis, spinal cord injury, allograft rejection, graft-versus-host disease, multiple sclerosis, Alzheimer's disease, etc. (see Tracy columns 1-2 and columns 21-22). Applicant differs from Tracey in that the stimulation comprises electrical stimulation of the sympathetic nervous system (versus electrical stimulation of the parasympathetic nervous system as taught by Tracey). The Examiner takes the position that it is conventional and well known in the art or neural stimulation that stimulation of either branch of the autonomic nervous system (i.e. either the parasympathetic branch or the sympathetic branch) may have the same effects on the body of a patient depending on the parameters of stimulation selected (i.e. low frequency for stimulation or high frequency for inhibition). One having ordinary skill in the art would know that if parasympathetic system is manipulated with electrical pulses to achieve a desired effect, then essentially the same effect could also be achieved with electrical pulses to the sympathetic system (except in a reciprocal fashion) and either choice is an obvious variant over the other. As supporting documentation the Examiner is submitting a few pages from a standard textbook of Human Physiology. On page 227 the paragraph beginning with there is an analogy of controlling heart rate with a person driving a car. Think of this like a person driving a car with one foot on the brake and the other foot on the accelerator. Either depressing the brake (parasympathetic) or relaxing the accelerator (sympathetic) will slow the car. The same rationale would apply to manipulating the inflammatory response of the body with either the parasympathetic or sympathetic division(s) using electrical stimulation.

30. As to Claims 15-17, see Tracey column 1, lines 28-34 and column 3, lines 6-18.

31. As to Claim 18, the Examiner takes the position that since the previously modified Tracey reference discloses a method for inhibiting the release of a pro-inflammatory cytokine such as IL-8, then the method also inherently inhibits the release of a pro-inflammatory chemokine (see column 6, lines 65-61). A chemokine is synonymous with various cytokines produced in acute and chronic inflammation that mobilize and activate white blood cells such as IL-8.

32. ***Claims 3-5, 23-24 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tracy in view of Sherwood as applied to claims 1-2 and 27 above, and further in view of Whitehurst et al. (U.S. 6,735,475) (herein Whitehurst).*** The previously modified Tracy reference discloses the claimed invention as discussed above except it is not specified that electrical pulses be provided to a sympathetic neuron/ganglia/postganglionic neuron via an implanted pulse generator. The Examiner takes the position that electrically modulating the sympathetic nervous system with electrical pulses using an implanted pulse generator is conventional and well known in the art with Whitehurst being but one example. Whitehurst discloses a small implantable stimulator, read as an implantable pulse generator 150 for applying electrical pulses to sympathetic ganglia or postganglionic neurons in order to interrupt or alter the inflammatory cytokine cascade in a patient (see Whitehurst Abstract, column 8, lines 10-56, column 10, lines 30-43, column 14, lines 43-56 and columns 16-19).

Double Patenting

33. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

34. Claims 1-18, 21-33, 35-36, 43-46, 48-53, 58-59, 61-63 and 68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-129 of copending Application No. 10/820,677. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are a

broadening of the scope of the claims presented in Application No. 10/820,677 or an obvious variant thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

35. Applicant's arguments with respect to claims 1 and 27 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

36. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure.

37. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

38. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica L. Reidel whose telephone number is (571) 272-2129. The examiner can normally be reached on Mon-Thurs 8:00-5:30, every other Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Pezzuto can be reached on (571) 272-6996. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jessica L. Reidel 01/31/07
Examiner
Art Unit 3766

Robert E. Pezzuto
Supervisory Patent Examiner
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